REMARKS

By the present amendment, claim 4 has been canceled without prejudice, claim 1 has been amended for purposes of readability, and new claims 22-27 have been added. Applicants reserve the right to prosecute the subject matter deleted from the amended claims and from the canceled claims in one or more related applications.

Both parts (ii) and (iv) of claim 1 have been amended to specify that the skin of a thermoplastic polyethylene vinylacetate copolymer covering the core contains 1 to 15 wt% vinylacetate, the skin being permeable for both compounds, and the skin has a thickness in the range of 10 to 110 μm. Support for the amendment to claim 1 can be found at, for example, page 5, lines 7-12.

Support for new claim 22 can be found at page 9, lines 31-32. Support for new claim 23 can be found at page 9, lines 32-33. Support for new claim 24 can be found at page 9, lines 33-35. Support for new claim 25 can be found at page 9, lines 35-36. Support for new claim 26 can be found at page 10, lines 34-35. Support for new claim 27 can be found at page 11, lines 1-2.

Applicants respectfully submit that the amendments to the claims and the new claims do not introduce any new matter.

After entry of the amendments, claims 1-3, 5-11, 13-16, and 21-27 will be pending.

I. The Presently Claimed Invention

Claim 1 has been amended in parts (ii) and (iv) to specify, *inter alia*, that the skin of the thermoplastic polyethylene vinylacetate copolymer contains 1 to 15 wt% vinyl acetate, and that the skin has a thickness of 10 to 110 μm. The use of such vinylacetate content in the skin and skin thickness results in an advantageous low burst release. *See* page 5, lines 10-14 of the present application. Furthermore, a skin thickness of less than about 110 μm is advantageous in obtaining good flexibility of the overall pharmaceutical delivery device.

Parts (ii) and (iv) of claim 5 specify, *inter alia*, that the skin of a thermoplastic polyethylene copolymer contains 14 to 28 wt% vinylacetate, and that the skin has a thickness of 70 to 250 um. With such vinylacetate content in the skin and skin thickness, obtaining a very good process consistency is especially easy. A skin of polyethylene vinylacetate copolymer with a vinylacetate content of about 14 to 28 wt% is further advantageous, because it results in an advantageously

lower extent of aging (*i.e.*, chemical or physical aging) of the material. In particular, such a configuration of the skin results in an advantageously low extent of change of the release profile of the active ingredients after long-term storage. *See* page 5, lines 15-29 of the present application.

II. The Claims are Patentable over EP 0866815

Claims 1-11, 13-16, and 21 are rejected under 35 U.S.C. 103(a) for allegedly being unpatentable over EP 0876815 (hereinafter "EP '815"). In particular, the Examiner contends that EP '815 strongly suggests concentration values at the saturation level at 25 °C, and that the instant claims are to concentrations just under the saturation level at 25 °C. According to the Examiner, the difference between the concentration values claimed by the Applicants, and those taught by EP '815 are different by a fraction of a wt%. The Examiner concludes that the ordinary artisan would not expect such a small change in concentration would result in different physical characteristics of the drug delivery system. In addition, the Examiner asserts that EP '815 provides sufficient guidance to the ordinary artisan to optimize the progestogenic steroid concentration range to find values just below the saturation level at 25 °C.

In view of the amendments and for the reasons set forth below, the Applicants respectfully disagree.

A. The Legal Standard

In its decision addressing the issue of obviousness, *KSR International Co. v. Teleflex Inc.*, 550 U.S. 398, 127 S.Ct. 1727, 82 U.S.P.Q.2d 1385 (2007), the Supreme Court stated that the following factors set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 U.S.P.Q. 459 (1966) still control an obviousness inquiry: (1) the scope and content of the prior art; (2) the differences between the prior art and the claimed invention; (3) the level of ordinary skill in the art; and (4) objective evidence of nonobviousness. *KSR*, 550 U.S. at 406 quoting *Graham*, 383 U.S. at 17-18, 14 U.S.P.Q. at 467; *see also* Examination Guidelines for Determining Obviousness Under 35 U.S.C. 103 in View of the Supreme court Decision in *KSR International Co. v. Teleflex Inc.* ("Examination Guidelines"), Federal Register, Vol. 72, No. 195, October 10, 2007, pages 57527-57528. The Supreme Court stated that in determining obviousness, "a court must ask whether the improvement is more than a predictable use of prior art elements according to their established functions." *KSR*, 550 U.S. at 417. The Supreme Court also stated that it is "important to identify a

reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does...." *KSR*, 550 U.S. at 418. The court reinforced this by stating that "a patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art. *Id.* This is consistent with the MPEP requirement that an Examiner must present a "convincing line of reasoning supporting a rejection."

In addition, obviousness cannot be predicated on what is not known at the time an invention is made, even if the inherency of a certain feature is later established. *In re Rijckaert*, 9 F.2d 1531, 28 USPQ2d 1955 (Fed. Cir. 1993). Determining whether an invention is obvious under 35 U.S.C. § 103, requires delineating the invention as a whole. This inquiry requires consideration of not only the subject matter which is literally recited in the claim in question but also those properties of the subject matter which are inherent in the subject matter and are disclosed in the specification. *In re Antonie*, 559 F.2d 619, 618, 195 USPQ 6 (CCPA 1977).

B. *Claims 1-3, 6-11, 13-16, and New Claims 22-25*

As noted above in Section I, claim 1 has been amended in parts (ii) and (iv) to specify, *inter alia*, that the skin of the thermoplastic polyethylene vinylacetate copolymer contains 1 to 15 wt% vinyl acetate, and that the skin has a thickness of 10 to 110 μm. The claimed drug delivery system has a relatively thin polyethylene vinylacetate copolymer skin with relatively low vinylacetate content. The claimed skin configuration results in an advantageously low burst release of active ingredient from the drug delivery system.

To examine the effects of the various design parameters including the vinylacetate content of the skin and the skin thickness on the burst release of the delivery system, the Applicants conducted the burst release study disclosed on pages 21 and 22 of the present application. Examples 2-4, 6-9, and 11-14 in Table IV on page 21, which have a relatively low vinylacetate content in the skin (*i.e.*, 9-15 wt.%) and which have a relatively thin skin (*i.e.*, 0.0036-0.0099 cm) all demonstrate lower burst release than do delivery systems such as Examples 5 and 10 which have a relatively higher vinylacetate content in the skin (*i.e.*, 20%) and which have a thicker skin *(i.e.*, 0.0134-0.0152 cm). Examples 2-4, 6-9, and 11-14, which meet the skin features specified in claim 1, also demonstrate lower burst release than the Nuvaring® Comparative Example which has an etonogestrel concentration above the saturation level.

In contrast to the Applicants' recognition that the vinylacetate content of the skin and skin thickness influence the burst release of the drug delivery system, EP '815 does not disclose this influence nor give reason to one of ordinary skill in the art to investigate these parameters in order to prevent burst release. This recognition which could only be realized by performing experiments which systematically vary vinylacetate content and skin thickness as discussed in the present application, is not disclosed in EP '815.

In addition, drug delivery systems having a skin thickness of 10 to 110 μm such as the drug delivery system specified in claim 1, show greater flexibility than systems having a greater skin thickness with the same overall thickness. For example, the Applicants invite the Examiner to compare the flexibilities of the systems of Examples 6, 7, and 9 with the flexibility of Example 10 in Table V at page 23 of the present application. Examples 6, 7, 9, and 10 have the same overall thickness and similar vinylacetate contents[1] in the core and skin, but have different skin thicknesses. Example 9, which has a skin thickness of 0.0099 cm and is a specific example of the system specified in claim 1, requires less force to bring about the specified deformation than is required for deforming Example 10 which has a relatively thicker skin of 0.0152 cm. Examples 6 and 7 require even less force to bring about the specified deformation because each of these systems have even thinner skins, *i.e.*, 0.0059 cm and 0.0047 cm, respectively.

In addition, Table V shows that the presently claimed systems are more flexible than the Nuvaring® comparative example which has an etonogestrel concentration above the saturation level. Example 12 and the Nuvaring® comparative example have the same fibre diameter and similar vinylacetate contents in the core and skin; however, Example 12 is considerably more flexible than is the Nuvaring® comparative example. The Applicants note that Example 12 has a much thinner skin (0.0036 cm) than the Nuvaring® comparative example (0.011 cm).

The improved flexibility gained from using a relatively thin skin in the drug delivery system results in improved comfort of for the end user. The improvements that result by employing a relatively thin skin in the system are not disclosed in EP '815. For these reasons, Applicants respectfully submit that EP '815 fails to render obvious claim 1, as amended.

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[1] The vinylacetate content of the skins in Examples 6, 7, 9 of 10 wt% or 15 wt% are lower than the 20 wt% in the skin of Example 10, and yet Examples 6, 7, and 9 show greater flexibility than does Example 10. This difference highlights even more the advantage of achieving greater flexibility with a system having a thinner skin, since systems having a higher vinylacetate content in the core show greater flexibility than do systems having a lower vinylacetate content in the core. *See* page 23, lines 5-7 of the present application.

Accordingly, in view of the amendments to claim 1, and for the reasons provided above, the Applicants respectfully submit that claim 1 is patentable over EP '815. Since claims 2, 3, 6-11, 13-16, and new claims 22-25 depend from claim 1, and include all the limitations of claim 1, the Applicants respectfully submit that these claims are also patentable over EP '815 for the same reasons. Applicants respectfully request reconsideration and withdrawal of the rejections of claims 1-3, 6-11, 13-16, and new claims 22-25.

C. *Claim 5 and New Claims 26-27*

As noted above in Section I, parts (ii) and (iv) of claim 5 specify, *inter alia*, that the skin of a thermoplastic polyethylene copolymer contains 14 to 28 wt% vinylacetate, and that the skin has a thickness of 70 to 250 um. The delivery system specified in claim 5, has a relatively thick polyethylene vinylacetate copolymer skin and relatively high vinylacetate content in the skin. Table VI at page 24 of the present application shows that drug delivery systems with a relatively thick skin and relatively high vinylacetate content show less aging, as measured by the change in the release of active ingredients after a given period after 5 months storage at 40 °C than do systems which have a thinner skin which contain a lower vinyl acetate content. For instance, the aging factors of 3.7% for Example 4 and 0% for Example 5 are lower than the aging factors for Examples 2 (7.3%) and 3 (5.3%), which are systems which have thinner skins and lower vinyl acetate contents than do Examples 4 and 5. Similarly improvement in the aging factors are also observed in comparing Examples 9 and 10 which have a relatively thick polyethylene vinylacetate copolymer skin and a high vinylacetate content in the skin, and Examples 7 and 8, which have thinner skins and a lower vinylacetate content in the skins than the system specified in claim 5.

In contrast to the Applicants' recognition that the vinylacetate content of the skin and its thickness influence the rate of aging of the drug delivery system, EP '815 does not disclose this influence nor give reason to one of ordinary skill in the art to investigate these parameters of the drug delivery system in order to prevent rapid aging and a change in the release rates of the active ingredients. For this reasons, Applicants respectfully submit that EP '815 fails to render obvious claim 5.

Accordingly, for the reasons provided above, the Applicants respectfully submit that claim 5 is patentable over EP '815. Since new claims 26 and 27 depend from claim 5, and include all the limitations of claim 5, the Applicants respectfully submit that these claims are also patentable over

EP '815 for the same reasons. Applicants respectfully request reconsideration and withdrawal of the rejections of claims 5, 26, and 27.

CONCLUSION

Entry of the foregoing amendments and remarks into the record of the above-identified application is respectfully requested. The Applicants submit that the amendments and remarks made herein now place the application in condition for allowance. If any other fee is necessary for consideration of this paper, please charge Deposit Account No. 50-4205. If any issues remain in connection herewith, the Examiner is respectfully invited to telephone the undersigned to discuss the same.

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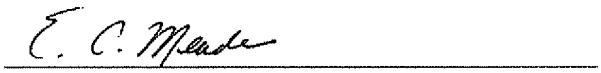
Respectfully submitted,



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